Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously Presented): A composition comprising a population of cytotoxic lymphocytes that is ex vivo expanded, wherein the expanded lymphocytes selectively damage tumor associated vasculature cells and wherein at least a subpopulation of the expanded lymphocytes express one or more members of a cell surface receptor family which binds at least heat shock protein 47, and a pharmaceutically acceptable carrier.

Claims 2-100: Cancelled.

101. (New): A composition comprising an ex vivo expanded population of cytotoxic lymphocytes identified as having the ability to kill tumor-associated vasculature cells, and a pharmaceutically acceptable carrier.

102. (New): The composition of claim 101, wherein at least a subclass of the ex vivo expanded population of cytotoxic lymphocytes selectively kill tumor-associated vascular endothelial cells as compared to physiologically normal vascular endothelia.

103. (New): The composition of claim 102, wherein the selectivity is at least two-fold.

104. (New): The composition of claim 102, wherein the ex vivo expanded population of cytotoxic lymphocytes exhibit lower toxicity to freshly confluent plated human umbilical cord endothelial cells in presence of Hsp47 than to freshly confluent plated human umbilical cord endothelial cells in the absence of Hsp47.

105. (New): The composition of claim 102, wherein the ex vivo expanded population of cytotoxic lymphoctes are less toxic to 5 day post-confluent plated human umbilical vein endothelial cells than to freshly confluent or non-confluent human umbilical vein endothelial cells.

106. (New): The composition of claim 105, wherein the ex vivo expanded population of cytotoxic lymphoctes are at least about two-fold less toxic to freshly-confluent human umbilical

vein endothelial cells in the absence of Hsp47 than in the presence of an optimal amount of Hsp47.

107. (New): The composition of claim 101, wherein the cytotoxic lymphocytes are expanded in a closed system.

108. (New): The composition of claim 107, wherein the cytotoxic lymphocytes are expanded in a bioreactor.

109. (New): The composition of claim 101, wherein the ex vivo expanded population of cytotoxic lymphoctes are immortalized.

110. (New): The composition of claim 101, wherein the ex vivo expanded cytotoxic lymphocytes comprise cells expressing both CD3 and CD56.

111. (New): The composition of claim 101, further comprising a chemotherapeutic compound.

112. (New): The composition of claim 101, further comprising an agent which binds to the cells non-covalently.

113. (New): The composition of claim 112, further comprising one or more of a toxin, a radioactive molecule, an immune modulator, a detectably labeled molecule and a tracer attached to the agent.

114. (New): The composition of claim 112 further comprising a toxin attached to the agent.

115. (New): The composition of claim 112, further comprising a radioactive molecule attached to the agent.

116. (New): The composition of claim 112, further comprising an immune modulator attached to the agent.

117. (New): The composition of claim 112, further comprising a tracer attached to the agent.

118. (New): The composition of claim 101, further comprising an antibody.

119. (New): The composition of claim 118, wherein the antibody is bound to a cell of the population of ex vivo expanded cytotoxic lymphocytes.

120. (New): The composition of claim 118, wherein the antibody is one of a mono-, bi- or multi-valent antibody.

121. (New): The composition of claim 118, further comprising one or more of a toxin, a radioactive molecule, an immune modulator, a detectably labeled molecule and a tracer attached to the antibody.

122. (New): The composition of claim 101, wherein the ex vivo expanded cytotoxic lymphocytes express one or more members of a cell surface receptor family, other than a T-cell Receptor, which further binds one or more of Hsp47, HLA-A, HLA-G, IL-12 receptor, and a polypeptide consisting of the amino acid sequence AVLSAEQRL (SEQ ID NO: 1)

123. (New): The composition of claim 122, wherein the member of a cell surface receptor family binds one of Hsp47 and a polypeptide consisting of the amino acid sequence AVLSAEQRL (SEQ ID NO: 1).

124. (New): The composition of claim 122, wherein the member of a cell surface receptor family binds HLA.

125. (New): The composition of claim 122, wherein the member of a cell surface receptor family recognizes binds IL-12 receptor.

126. (New): The composition of claim 122, wherein the member of the cell-surface receptor is a killer inhibitory receptor.

127. (New): The composition of claim 122, wherein the member of the cell-surface receptor is an inhibitory receptor.

128. (New): The composition of claim 101, further comprising dendritic cells, T helper cells, T_{CTL} cells, NK cells or tumor targets or extracts thereof.

129. (New): The composition of claim 128, comprising dendritic cells pulsed with tumor or endothelial antigens.

130. (New): The composition of claim 128, comprising unpulsed dendritic cells.

131. (New): The composition of claim 101, wherein the ex vivo expanded cytotoxic lymphocytes are not lethally irradiated.

132. (New): The composition of claim 101, further comprising an additional cytokine.

133. (New): The composition of claim 101, wherein the ex vivo expanded cytotoxic lymphocytes are not stably transfected with a nucleic acid molecule encoding a cytokine.

134. (New): The composition of claim 101, wherein the ex vivo expanded cytotoxic lymphocytes are frozen.

135. (New): The composition of claim 134, packed within a shipping package.

136. (New) The composition of claim 101, wherein the cytotoxic lymphocytes are ex vivo expanded in the absence of tumor or vasculature associated antigen.

137. (New): The composition of claim 101, comprising a number of cells effective to treat a cancer in a patient.

138. (New): The composition of claim 137, comprising greater than about 10^4 cells.

139. (New): The composition of claim 137, comprising greater than about 10^8 cells.

140. (New): The composition of claim 101, wherein the composition is suitable for human use in quantities of at least about 10^4 cells per dose.

141. (New): The composition of claim 140, wherein the composition is suitable for use in humans in quantities of at least about10^8 cells per dose.

142. (New): A composition comprising a population of ex vivo expanded cytotoxic lymphocytes quantitated for their antiangiogenic activity.

143. (New): A composition comprising a population of ex vivo expanded lymphocytes wherein the ex vivo expanded cytotoxic lymphocytes are selected to kill freshly confluent cultured human umbilical cord endothelial cells in a non-MHC Class I-restricted manner, in the absence of Hsp47, and a pharmaceutically acceptable carrier.

144. (New): A composition comprising a population of ex vivo expanded cytotoxic lymphocytes, wherein the ex vivo expanded cytotoxic lymphocytes do not cause vascular leak syndrome and are identified as having the ability to kill neo-vascular cells.

145. (New): A composition comprising a population of ex vivo expanded non-MHC Class I - restricted cytotoxic lymphocytes identified as having the ability to kill cells in neo-vasculature, wherein the cytotoxic lymphocytes do not express a T cell receptor.

146. (New): A composition comprising a population of cytotoxic lymphocytes expanded in a bioreactor or closed system, wherein the composition is safe for human cellular therapy.

147. (New): The composition of claim 146, wherein the lymphocytes are cytotoxic lymphocytes able to kill cells in neo-vasculature.

148. (New): The composition of claim 146, wherein the cells are safe for human use in a cellular immunotherapy at a dose of greater than about 10^4 cells.

149. (New): The composition of claim 146, wherein the cells are safe for human use in a cellular immunotherapy at a dose of greater than about 10^8 cells.

150. (New): The composition of claim 146, wherein, subsequent to the expansion, the cells are titrated for anti-neo-vasculature or antitumor activity to produce a unit dosage of cells.

151. (New): The composition of claim 146, wherein, subsequent to the expansion, the cells are titrated for lack of clinically significant activity against non-tumor-associated or physiologically normal vascular cells.

152. (New): A composition comprising a population of cytotoxic lymphocytes that is ex vivo expanded in absence of tumor or vasculature antigen, wherein the ex vivo expanded lymphocytes selectively damage tumor associated vasculature cells, and a pharmaceutically acceptable carrier.

153. (New): The composition of claim 152, further comprising one of an antibody and an agent which binds to the ex vivo expanded lymphocytes non-covalently.

154. (New): The composition of claim 152, comprising an agent which binds to the ex vivo expanded lymphocytes non-covalently.

155. (New): The composition of claim 154, further comprising one or more of a toxin, a radioactive molecule, an immune modulator, a detectably labeled molecule and a tracer attached to the agent.

156. (New): The composition of claim 154, wherein the agent is a protein that binds the ex vivo expanded cytotoxic lymphocytes and directs the cytotoxic lymphocytes to a tumor target.

157. (New): The composition of claim 154, wherein the agent is protein that binds the ex vivo expanded cytotoxic lymphocytes and directs the cytotoxic lymphocytes to a tumor associated vasculature target.

158. (New): A composition comprising a population of cytotoxic lymphocytes prepared according to a process, comprising:

a) ex vivo expanding peripheral blood lymphocytes in a closed system; and

b) determining if, and to which extent, a population of cytotoxic lymphocytes among the ex vivo expanded peripheral blood lymphocytes can kill cells in neo-vasculature.

159. (New): The composition of claim 158, wherein toxicity to sub-confluent or freshly confluent plated human umbilical vein endothelial cells is used to determine determining if a population of cytotoxic lymphocytes among the ex vivo expanded peripheral blood lymphocytes can kill cells in neo-vasculature.

160. (New): The composition of claim 158, further comprising determining if, and to which extent, the population of cytotoxic lymphocytes among the ex vivo expanded peripheral blood lymphocytes can selectively kill neo-vasculature as compared to normal vasculature.

161. (New): The composition of claim 158, wherein determining if, and to which extent, the population of cytotoxic lymphocytes among the ex vivo expanded peripheral blood lymphocytes can selectively kill neo-vasculature as compared to normal vasculature is performed by one of:

a) comparing relative toxicity of the cytotoxic lymphocytes to sub-confluent or freshly confluent human umbilical vein endothelial cells as compared to human umbilical vein endothelial cells that are confluent; and

b) comparing relative toxicity of the cytotoxic lymphocytes to sub-confluent or freshly confluent human umbilical vein endothelial cells in the presence and absence of Hsp47 or a polypeptide containing the amino acid sequence AVLSAEQRL (SEQ ID NO: 1).

162. (New): The composition of claim 158, wherein the lymphocytes are expanded in the presence of interferon gamma, anti-CD3 antibody, and interleukin-2.

163. (New): The composition of claim 158, wherein the closed system is a bioreactor.

164. (New): The composition of claim 163, wherein the bioreactor includes electrodes.

165. (New): The composition of claim 158, further comprising agitating the lymphocytes.

166. (New): The composition of claim 158, further comprising aerating the lymphocytes.

167. (New): The composition of claim 158, further comprising non-continually adding new medium to the culture.

168. (New): The composition of claim 158, wherein the cells are titrated for anti-neo-vasculature or antitumor activity to produce a unit dosage of cells.

169. (New): The composition of claim 168, wherein the unit dosage comprises a number of cells effective to treat a cancer in a patient.

170. A composition comprising ex vivo expanded cytotoxic lymphocytes having the ability to kill tumor-associated vasculature cells in an amount effective to treat a cancer in a human patient, wherein the composition does not produce vascular leak syndrome in the human patient.

171. The composition of claim 170, comprising at least about 10^4 cells.

172. The composition of claim 170, comprising at least about 10^8 cells.